

牛尾草中一新的对映 – 贝壳杉烷型二萜

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摘要: 从牛尾草 [*Isodon ternifolius* (D. Don) Kudo] 的地上部分分离得到一个新的对映 – 贝壳杉烷型二萜, 命名为牛尾草素 H (1), 通过波谱方法鉴定了它的结构。此外, 还分离得到 5 个已知的对映 – 贝壳杉烷型二萜化合物: 香茶菜醛 (2), 长管香茶菜素 A , E 和 G (3 – 5), 开展香茶菜素 E (6), 以及木樨草素 (7), 芹菜素 (8), α – 香树脂醇 (9), 乌索酸 (10) 和 2α – 羟基乌索酸 (11)。

关键词: 牛尾草 ; 唇形科 ; 对映 – 贝壳杉烷型二萜 ; 牛尾草素 H

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A New *ent*-Kauranoid from *Isodon ternifolius*

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Abstract : A new *ent*-kauranoid named rabdoternin H (1) was isolated from the aerial part of *Isodon ternifolius* and its structure was determined by the spectroscopic methods. Five known *ent*-kaurane diterpenoids, isodonal (2), longikaurin A , E , G (3 – 5) and effusanin E (6), together with luteolin (7), apigenin (8), α -amyrin (9), ursolic acid (10) and 2α -hydroxy-ursolic acid (11) were also reported in this paper.

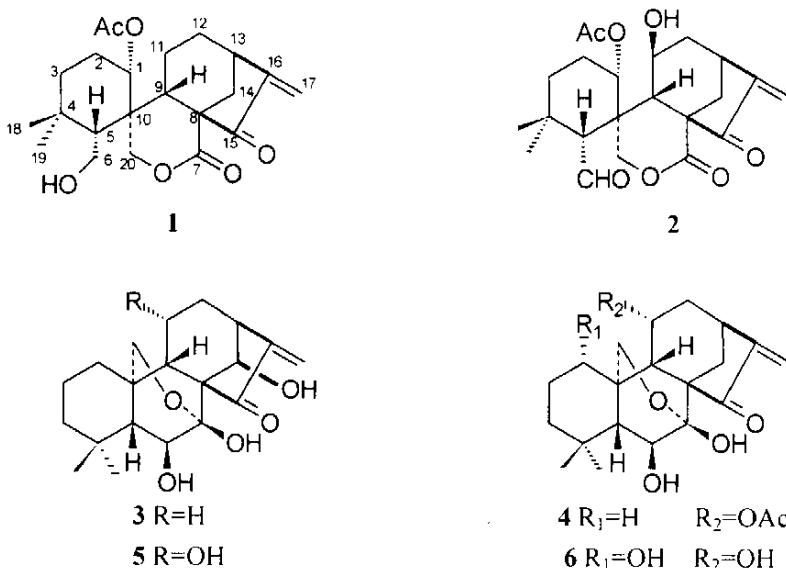
Key words : *Isodon ternifolius* ; Labiateae ; *ent*-Kauranoid ; Rabdoternin H

Isodon ternifolius (D. Don) Kudo , a perennial herb or shrub mainly distributed in Yunnan , Guizhou , Guangdong and Guangxi Province , has been used to treat dysenteric enteritis , pharyngitis , tonsillitis etc (Wu et al , 1977). A series of *ent*-kaurane diterpenoids from this plant have been reported previously (Sun et al , 1982 ; Takeda et al , 1990 ; Takeda et al , 1994). Our re-investigation on this plant led to the isolation of a new *ent*-kaurane diterpenoid , rabdoternin H (1) and ten known compounds , isodonal (2)(Sun et al , 1982), longikaurin A (3)(Takeda et al , 1988a), longikaurin E (4)(Sun et al , 1982), longikaurin G (5)(Takeda et al , 1988b), effusanin E (6)(Wang et al ,

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1989), luteolin (7) (Markham *et al*, 1978), apigenin (8) (Markham *et al*, 1978), α -amyrin (9) (Mahato *et al*, 1994), ursolic acid (10) and 2 α -hydroxy-ursolic acid (11).

Rabdoterin H (1), colorless needles, showed an EIMS molecular ion peak at m/z 390 in accordance with the formula $C_{22}H_{30}O_6$, which was confirmed by analysis of its ^{13}C NMR (DEPT) spectra. It possessed an *exo*-methylene group conjugated with a carbonyl group on a five-membered ring from the following spectral data: UV $\lambda_{\max}^{\text{MeOH nm}}$: 232.0; IR $\nu_{\max}^{\text{KBr cm}^{-1}}$: 1712 and 1648; 1H NMR: δ 5.95 and 5.33 (each 1H, brs); ^{13}C NMR: δ 118.3 (CH_2), 151.4 (C) and 202.5 (C). In addition to the above-mentioned signals, the ^{13}C NMR spectrum also showed the presence of an acetoxy group, two methyl, seven methylenes (including two oxygenated ones), four methines (including one oxygen-bearing one), three quaternary carbons and a lactone carbonyl group. With consideration of the types of diterpenoids in the *Isodon* genus, these facts indicated that 1 was an *ent*-kauranoid.

There were no correlations between H-5, H-6 and C-7; H-1 and C-7 in HMBC spectrum, which indicated the basic skeleton of 1 was 6, 7-*seco*-spiro-lacton-*ent*-kauranoid. The NOE effects (H-20a with Me-19, H-5 β with H-9 β) also confirmed the presumption. On the basis of 1H - 1H COSY spectrum, a hydroxyl was assigned to C-6. The acetoxy was assigned to C-1, because the methine at δ 77.1 (C-1) and the correlation between H-1 and the ester carbonyl at δ 170.2 in HMBC spectrum were observed. The acetoxy group was judged to be α -orientated due to the observation of NOE effects between H-1 and H-5 β , H-11. In conclusion, rabdoterin H (1) was elucidated as 1 α -acetoxy-6-hydroxy-6, 7-*seco*-*ent*-kaur-16-en-15-one-7, 20-olide.

Compounds 2-9 were identified as isodonol (2), longikaurin A, E, G (3-5), effusinan E (6), luteolin (7), apigenin (8), α -amyrin (9), ursolic acid (10) and 2 α -hydroxy-ursolic acid (11), respectively, by comparing their physical and spectral data with those reported in the literature.

Experimental

General Melting point was measured on an XRC - 1 micro melting point apparatus and uncorrected. Optical rotation was taken on a SEPA - 300 polarimeter. IR spectral data was measured on a Bio-Rad FTS - 135 spectrometer with KBr pellets. UV spectra was obtained on a UV 210A spectrometer. MS spectra were recorded on a VG Auto Spec-3000 spectrometer. NMR spectra were run on a Bruker AM - 400 and a DRX - 500 instrument with TMS as internal standard.

Extraction and Isolation Plant material was collected in Malipo County of Yunnan Province in October, 1994, and identified as *Isodon ternifolius* (D. Don) Kudo by Prof. Zhong-Wen Lin. A voucher specimen was deposited in the Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences.

The air-dried and powdered plants (8.0 kg) were extracted with 70% acetone at room temperature for 3 days each time. The extract was concentrated and filtered, and the filtrate was partitioned with petroleum-ether and EtOAc successively. The EtOAc extract (109 g) was subjected to column chromatography on a Si gel column and eluted with CHCl₃ containing increasing amounts of Me₂CO system to give six fractions (I-VI). Fractions I-V were further purified by repeated column chromatography on Si gel and recrystallization to yield compounds **1** (23 mg), **2** (21 mg), **3** (37 mg), **4** (35 mg), **5** (43 mg), **6** (1.2 g), **7** (21 mg), **8** (11 mg), **9** (23 mg), **10** (5 g) and **11** (137 mg).

Table 1 ¹H, ¹³C NMR, ¹H-¹H COSY and HMBC data of **1** in C₅D₅N

¹³ C NMR (125 MHz)		¹ H NMR (500 Hz)		HMBC
C	δ (mult)	H	δ (mult , J in Hz)	(H to C)
1	77.1 (d)	1 β	5.01 (m)	2 20, OAc
2	24.4 (t)	2 α , β	1.88 (m)	1, 3 1, 3
3	40.0 (t)	3 α , β	1.38 (m)	2 1, 2, 4
4	33.9 (s)	5 β	1.72 (br s)	6a, 6b 4, 6
5	53.6 (d)	6a	3.83 (overlap)	5, 6b 4, 5, 10
6	58.9 (t)	6b	3.80 (overlap)	5, 6a 4, 5, 10
7	170.9 (s)	9 β	3.21 (d, 13.1)	11 α 1, 5, 7, 8, 9, 10, 11, 12, 14, 15
8	58.7 (s)	11 α	1.40 (m)	9, 11 β 8, 9, 12
9	42.3 (d)	11 β	1.85 (m)	11 α 8, 9, 10, 12, 13
10	44.4 (s)	12 α	1.99 (m)	12 β , 13 α 9, 11, 13, 14, 16
11	17.9 (t)	12 β	1.34 (m)	12 α 14, 16
12	30.2 (t)	13 α	2.91 (m)	12 α , 14 β 8, 11, 15, 16, 17
13	35.3 (d)	14 α	2.15 (overlap)	14 β 7, 8, 9, 12, 13, 15
14	29.3 (t)	14 β	2.58 (dd, 4.4, 12.3)	13 α , 14 α 8, 9, 12, 13, 15, 16, 17
15	202.5 (s)	17a	5.95 (br s)	17b 13, 15, 16
16	151.4 (s)	17b	5.33 (br s)	17a 13, 15
17	118.3 (t)	Me - 18	0.99 (s)	3, 4, 5, 19
18	33.6 (q)	Me - 19	0.78 (s)	3, 4, 5, 18
19	23.6 (q)	20a	5.12 (ABd, 12.2)	20b 1, 7, 9
20	68.9 (t)	20b	4.84 (ABd, 12.2)	20a 1, 9
OAc	170.2 (s), 21.5 (q)	OAc	2.17 (s)	1

Rabdotermin H (**1**) , C₂₂H₃₀O₆ ; colorless needles (MeOH); mp 246 – 248°C ; [α]_D^{24.9} + 36.3° (c 0.903, MeOH); UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log_e): 232.0 (3.87); IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹ : 3415, 2948, 1740, 1712, 1648, 1447, 1407, 1366, 1293, 1267, 1233, 1188, 1046; EI-MS (70eV) m/z (%): 390 [M]⁺ (78), 362 (18), 348 (15), 330 [M-AcOH]⁺ (23), 312 (20), 284 (21),

257(30), 239(26), 227(31), 192(16), 178(31), 133(48), 119(40), 105(69), 91(100), 81(65); ^1H and ^{13}C NMR data see Table 1.

Isodonal (**2**), $\text{C}_{22}\text{H}_{28}\text{O}_7$; colorless needles (MeOH); EI-MS (70eV) m/z (%): 404 [M]⁺ (25), 386 [M-H₂O]⁺ (9), 344 [M-AcOH]⁺ (100), 326 [M-AcOH-H₂O]⁺ (12), 316 (28), 298 (23), 270 (20), 245 (87), 227 (57), 217 (52), 149 (67), 81 (70); ^1H NMR (500 MHz, $\text{C}_5\text{D}_5\text{N}$) δ : 10.01 (1H, d, J =1.8 Hz, CHO), 6.03 and 5.40 (each 1H, s, H₂-17), 5.51 (1H, m, H-1 β), 5.44 and 5.22 (each 1H, ABd, J =12.4 Hz, H₂-20), 4.41 (1H, m, H-11 α), 2.93 (1H, d, J =4.5 Hz, H-5 β), 2.15 (3H, s, OAc), 0.98 and 0.95 (each 3H, s, 2×Me); ^{13}C NMR (125 MHz, $\text{C}_5\text{D}_5\text{N}$) δ : 204.9 (d, C-6), 200.8 (s, C-15), 170.3 (s, C-7), 150.6 (s, C-16), 119.3 (t, C-17), 76.0 (d, C-1), 67.1 (t, C-20), 65.2 (d, C-11), 61.2 (d, C-5), 58.5 (s, C-8), 46.8 (d, C-9), 44.6 (s, C-10), 41.4 (t, C-12), 40.2 (t, C-3), 34.6 (d, C-13), 34.5 (s, C-4), 33.2 (q, C-18), 29.9 (t, C-14), 24.5 (q, C-19), 24.4 (t, C-2), OAc: 170.3, s, 21.4, q.

Longikaurin A (**3**), $\text{C}_{20}\text{H}_{28}\text{O}_5$; colorless needles (MeOH); EI-MS (70eV) m/z (%): 348 [M]⁺ (83), 330 [M-H₂O]⁺ (35), 319 (16), 302 (45), 284 (22), 269 (20), 217 (39), 177 (36), 167 (60), 151 (83), 133 (43), 109 (58), 85 (68); ^1H NMR (500 MHz, $\text{C}_5\text{D}_5\text{N}$) δ : 6.86 (1H, d, J =10.0 Hz, OH-6 β), 6.26 and 5.50 (each 1H, s, H₂-17), 5.11 (1H, s, H-14 α), 4.16 (1H, dd, J =10.0, 6.3 Hz, H-6 α), 4.13 and 3.93 (each 1H, ABd, J =10.0 Hz, H₂-20), 3.15 (1H, d, J =9.5 Hz, H-13 α), 1.23 and 1.04 (each 3H, s, 2×Me); ^{13}C NMR (125 MHz, $\text{C}_5\text{D}_5\text{N}$) δ : 208.8 (s, C-15), 153.0 (s, C-16), 119.6 (t, C-17), 98.4 (s, C-7), 74.2 (d, C-6), 73.6 (d, C-14), 66.3 (t, C-20), 62.7 (s, C-8), 60.8 (d, C-9), 52.5 (d, C-5), 43.9 (d, C-13), 41.5 (t, C-3), 36.5 (s, C-10), 34.0 (s, C-4), 33.7 (q, C-18), 30.7 (t, C-1), 30.2 (t, C-12), 22.4 (q, C-19), 19.0 (t, C-11), 16.7 (t, C-2).

Longikaurin E (**4**), $\text{C}_{22}\text{H}_{30}\text{O}_6$; colorless needles (MeOH); EI-MS (70eV) m/z (%): 390 [M]⁺ (100), 372 [M-H₂O]⁺ (4), 330 [M-AcOH]⁺ (35), 312 [M-AcOH-H₂O]⁺ (30), 284 (27), 269 (18), 255 (13), 227 (10), 213 (14), 200 (16), 179 (16), 151 (35), 120 (24); ^1H NMR (500 MHz, $\text{C}_5\text{D}_5\text{N}$) δ : 6.61 (1H, d, J =11.0 Hz, OH-6 β), 5.99 and 5.30 (each 1H, s, H₂-17), 5.43 (1H, t, J =4.5 Hz, H-11 β), 4.40 and 4.22 (each 1H, ABd, J =9.2 Hz, H₂-20), 4.30 (1H, dd, J =11.0, 7.5 Hz, H-6 α), 2.07 (3H, s, OAc), 1.28 and 1.06 (each 3H, s, 2×Me); ^{13}C NMR (125 MHz, $\text{C}_5\text{D}_5\text{N}$) δ : 209.7 (s, C-15), 153.1 (s, C-16), 117.2 (t, C-17), 96.2 (s, C-7), 75.0 (d, C-6), 68.8 (d, C-11), 68.7 (t, C-20), 60.1 (d, C-9), 59.2 (s, C-8), 53.4 (d, C-5), 41.7 (t, C-3), 38.0 (t, C-12), 37.2 (s, C-10), 34.5 (t, C-1), 34.2 (q, C-18), 33.9 (s, C-4), 31.2 (d, C-13), 27.7 (t, C-14), 22.8 (q, C-19), 18.8 (t, C-2), OAc: 169.8, s, 21.6, q.

Longikaurin G (**5**), $\text{C}_{20}\text{H}_{28}\text{O}_6$; colorless needles (MeOH); EI-MS (70eV) m/z (%): 364

$[M]^+$ (68), 346 [$M-H_2O]^+$ (51), 328 (12), 315 (31), 300 (17), 269 (10), 215 (17), 175 (24), 167 (42), 151 (69), 136 (36), 123 (43), 109 (57), 85 (100), 69 (74); 1H NMR (500 MHz, C_5D_5N) δ : 6.79 (1H, d, $J=11.0$ Hz, OH- 6β), 6.39 (1H, s, H- 14α), 6.27 and 5.50 (each 1H, s, H₂-17), 5.16 and 4.29 (1H, ABd, $J=8.6$ Hz, H₂-20), 4.40 (1H, m, H- 11β), 4.31 (1H, dd, $J=7.5, 11.0$ Hz, H- 6α), 1.40 (1H, d, $J=7.5$ Hz, H- 5β), 1.32 and 1.11 (each 3H, s, $2\times$ Me); ^{13}C NMR (125 MHz, C_5D_5N) δ : 209.4 (s, C-15), 153.5 (s, C-16), 118.7 (t, C-17), 98.9 (s, C-7), 75.1 (d, C-14), 72.5 (d, C-6), 69.2 (t, C-20), 65.2 (d, C-11), 63.0 (s, C-8), 60.0 (d, C-9), 56.4 (d, C-5), 43.5 (d, C-13), 42.7 (t, C-12), 41.5 (t, C-3), 37.6 (s, C-10), 34.6 (q, C-18), 34.0 (s, C-4), 31.2 (t, C-1), 23.0 (q, C-19), 19.0 (t, C-2).

Effusanin E (**6**), $C_{20}H_{28}O_6$; colorless needles (MeOH); EI-MS (70eV) m/z (%): 364 [$M]^+$ (76), 346 [$M-H_2O]^+$ (8), 300 (8), 285 (10), 267 (9), 259 (10), 229 (12), 192 (16), 179 (18), 161 (31), 149 (24), 135 (30), 121 (42), 107 (45), 95 (50), 85 (75); 1H NMR (500 MHz, C_5D_5N) δ : 6.88 (1H, d, $J=11.0$ Hz, OH- 6β), 5.95 and 5.28 (each 1H, s, H₂-17), 5.18 and 4.37 (each 1H, ABd, $J=9.4$ Hz, H₂-20), 4.57 (1H, br s, H- 11β), 4.33 (1H, dd, $J=11.0, 7.0$ Hz, H- 6α), 3.87 (1H, dd, $J=10.0, 6.2$ Hz, H- 1β), 3.68 (1H, d, $J=11.6$ Hz, H- 14α), 1.31 and 1.12 (each 3H, s, $2\times$ Me); ^{13}C NMR (125 MHz, C_5D_5N) δ : 211.4 (s, C-15), 154.5 (s, C-16), 115.3 (t, C-17), 96.3 (s, C-7), 75.4 (d, C-1), 73.5 (d, C-6), 67.0 (d, C-11), 65.7 (t, C-20), 60.9 (d, C-5), 60.0 (s, C-8), 55.1 (d, C-9), 43.1 (s, C-10), 39.4 (t, C-3 and 12), 34.9 (q, C-18), 34.0 (s, C-4), 33.8 (d, C-13), 29.4 (t, C-2), 27.1 (t, C-14), 22.5 (q, C-19).

Luteolin (**7**), $C_{15}H_{10}O_6$; yellow powder; EI-MS (70eV) m/z (%): 286 [$M]^+$ (100), 258 (20), 229 (10), 153 [$A_1+1]^+$ (31), 134 [$B_1]^+$ (16), 69 (15). Its 1H and ^{13}C NMR data are consistent with those of luteolin reported in the literature (Markham *et al*, 1978).

Apigenin (**8**), $C_{15}H_{10}O_5$; yellow powder; EI-MS (70eV) m/z (%): 270 [$M]^+$ (100), 242 (31), 213 (7), 153 [$A_1+1]^+$ (31), 121 [$B_1]^+$ (35), 96 (11), 69 (26). Its 1H and ^{13}C NMR data are consistent with those of apigenin reported in the literature (Markham *et al*, 1978).

α -Amyrin (**9**), $C_{30}H_{50}O$; white powder; EI-MS (70eV) m/z (%): 426 [$M]^+$ (18), 411 (4), 218 (100), 203 (27), 189 (16), 161 (9), 149 (20), 135 (21), 81 (24), 69 (33), 55 (37). Its 1H and ^{13}C NMR data are consistent with those of α -amyrin reported in the literature (Mahato *et al*, 1994).

Ursolic acid (**10**), $C_{30}H_{48}O_3$; white powder; EI-MS (70eV) m/z data and Rf value on TLC are consistent with those of authentic sample.

2 α -Hydroxy-ursolic acid (**11**), $C_{30}H_{48}O_4$; white powder; EI-MS (70eV) m/z data and Rf value on TLC are consistent with those of authentic sample.

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